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Advances in Conditioning Regimens

New, less intense conditioning regimens are being used today that retain the desirable effects of standard high-dose conditioning regimens, but with significantly lower transplant-related mortality (TRM).

Non-myeloablative and reduced-intensity conditioning regimens have also expanded the number of patients eligible to receive hematopoietic cell transplants.

Non-Myeloablative Regimens

Non-myeloablative regimens use significantly lower doses of pre-transplant chemotherapy drugs and/or radiation than the traditional high-dose, myeloablative regimens that have been in use for more than 35 years. Non-myeloablative regimens do not attempt to completely eliminate malignant cells prior to transplant, but instead rely upon a graft-versus-malignancy effect mediated by donor-origin T cells. [1]

Non-myeloablative transplants have expanded the number of patients eligible for hematopoietic cell transplantation. Due to its lowered toxicity, non-myeloablative transplants can be appropriate for:

- Patients older than 55 years, which is a common upper limit for standard myeloablative transplantation
- Patients with one or more co-morbidities that would ordinarily exclude them from undergoing myeloablative transplantation

Although long-term follow-up data are not yet available, lower TRM and reduced rates of acute and chronic GVHD have been achieved in older patients and in patients with co-morbidities receiving non-myeloablative transplants, with rates comparable to those achieved by younger transplant patients. [2]

Clinical studies of non-myeloablative transplantation have shown that the graft-versus-malignancy effect is particularly pronounced in:

- Chronic myelogenous leukemia
- Chronic lymphocytic leukemia
- Low-grade, non-aggressive lymphomas [1]

Autologous transplant followed by non-myeloablative allogeneic transplantation is also being investigated by several groups. This treatment strategy attempts to combine the tumor cytoreduction of a high-dose autologous transplant with the lowered TRM of a non-myeloablative conditioning regimen with an allogeneic transplant. This technique has been particularly successful in treating patients with multiple myeloma. [3]

Reduced-Intensity Regimens

These regimens use combinations of chemotherapy drugs such as fludarabine, busulfan, ATG, and melphalan. They are not fully myeloablative, but they use higher doses than non-myeloablative regimens.

Initial reports have shown that reduced-intensity regimens have acceptable remission rates and lower overall rates of toxicity compared to standard high-dose therapy. [1,4] Rates of acute and chronic GVHD after reduced-intensity regimens are comparable to those observed in standard high-dose transplants, but the onset of GVHD is often delayed by weeks to months. [5]

Myeloablative Regimens

Despite the many successes in reducing the intensity of conditioning regimens, fully myeloablative regimens are still used for the majority of patients undergoing hematopoietic cell transplantation.

High-dose regimens are particularly useful in conditioning patients with aggressive malignancies, where there is a need for a strong anti-leukemia or anti-tumor effect.

Cyclophosphamide plus total body irradiation (TBI) and cyclophosphamide plus busulfan are typical approaches for fully myeloablative regimens, but combining busulfan with fludarabine is increasing in use. [6, 7]

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